Against the tide

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Although the methods and the results seem to flow against the tide of the current literature,¹ the article by Zheng and colleagues² published in this issue of the *Journal* has several merits. In fact, multidisciplinary teams, especially in North America, tend to consider primary treatment for locally advanced non–small cell lung cancer as nonsurgical, although N2 disease is being resected worldwide for various indications.³ In this setting, a list of the important issues that have been raised by the contribution by Zheng and colleagues² can be identified.

First, avoid preresection mediastinal exploration. In this series, patients underwent resection on the basis of evidence of mediastinal involvement at computed tomographic imaging, with positron-emission tomography reserved for bulky N2 disease. In fact, mediastinoscopy, endobronchial ultrasound, and endoscopic ultrasound were not used to stage the mediastinum of surgical candidates. The concept of avoiding preresectional mediastinal exploration to proceed directly to complete nodal dissection during primary surgery has already emerged in the literature after decades when meticulous mediastinal (invasive) staging has been required to avoid surgery.⁴ Because of this lack of imaging, complete nodal dissection is a crucial component of the upfront surgical approach, especially when the nonnegligible prevalence of N2 disease in patients with T1 disease is considered.²

Second, use surgery first, but not surgery alone. In the interpretation of outcomes originating from upfront resection for N2, one misunderstanding is that surgery should be performed as the only therapeutic modality. This series by Zheng and colleagues² clearly shows that surgery should be rather followed by adjuvant treatment, even if it may be difficult to separate the relative impacts of each modality on overall and progression-free survivals. In this context, the impact of the surgical arm in multimodality treatment trials has been recently emphasized, paving the way to considering upfront surgery.⁵ Moreover, recent evidence demonstrates that chemotherapy is the adjuvant treatment of choice after complete resection of unsuspected N2 disease,

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Central Message

It is time to reconsider the role of upfront surgery in the multimodality treatment of locally advanced non–small cell lung cancer.

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because radiotherapy was not associated with a survival benefit.⁶

Third, lymphadenectomy is linked to survival. Zheng and colleagues² have reported on a large series of patients with primarily resected clinical stage IIIA disease, confirming Liang and colleagues' finding that improved survivals may be related to removing at least 16 lymph nodes per patient⁷—in the series of Zheng and colleagues,² an average of 20 per patient. Although the thoracic surgical community still lives in the aftermath of the results from American College of Surgery Oncology Group Z0030, which clearly argue against any survival improvement associated with complete lymphadenectomy,⁸ the article by Zheng and colleagues² is an invitation to reconsider the role of surgery as a means of effecting optimal staging and potentially improving survival of patients with lung cancer.⁷

Finally, N2 subsets are associated with survival. Zheng and colleagues' series² confirms the recurring reports in the literature demonstrating the particularly favorable prognostic outlook associated with either occult or single-station N2 subsets.⁹⁻¹¹ In the article by Zheng and colleagues,² these N2 subgroups were associated with overall and progression-free survivals in excess of 50% and 25%, respectively. Moreover, when one considers the whole pIIIA-N2 group, the median progression-free survival of 17.0 months (14 months for cN2) and the median overall survival of 44.0 months (35 months for cN2) should suggest a careful reevaluation of the multimodality

strategy to be used in patients with N2 non–small cell lung cancer.²

Although the limitations of this study are manifold and have been adequately presented by Zheng and colleagues² themselves, the value of this contribution remains significant, inasmuch as it shines a new light on the important role of surgery in the management of locally advanced lung cancer. In this setting, the analysis of the resected mediastinal nodes may also add important information on the immunohistochemical profile of the tumor, thus contributing to finalizing the prognostic outlook.¹² In a time when old standards of care in oncology are being questioned,¹³ thoracic surgeons should be ready to swim against the tide to propose and collaborate on new clinical trials focused on primary surgery for locally advanced lung cancer.

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